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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,909	12/06/2001	Jay Keasling	2000-0007	1524

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EXAMINER

FRONDA, CHRISTIAN L

ART UNIT PAPER NUMBER

1652

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/006,909

<b>Applicant(s)</b>	
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KEASLING ET AL.

**Examiner**

Christian L. Fronda

<b>Art Unit</b>
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**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 08 September 2006.  
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-11,13-21,23,61-85 and 87-102 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11,13-21,23,61-85 and 87-102 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 12/05, 05/06.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.  
5) ☐ Notice of Informal Patent Application  
6) ☐ Other: \_\_\_\_\_

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### DETAILED ACTION

1. Claims 1-11, 13-21, 23, 61-85, and 87-102 are pending and under consideration in this Office Action. New rejections and new grounds of rejection are presented in this instant Office Action.
2. The rejection of claims 1, 3, 4, 6-8, 10, 12-14, 23 under 35 U.S.C. 103(a) as being unpatentable over Takagi et al. (J Bacteriol. 2000 Aug;182(15):4153-7; reference of record) in view of Hiser et al. (J Biol Chem. 1994 Dec 16;269(50):31383-9, and Accession L20428; PTO892) and Wang et al. (Accession AF119715. 22-April-1999; reference of record) has been withdrawn in view of applicants' amendments and arguments filed 09/08/2006.
3. The rejection of claim 2 under 35 U.S.C. 103(a) as being unpatentable over Takagi et al. in view of Hiser et al. and Wang et al. as applied to claims 1, 3, 4, 6-8, 10, 12-14, 23; and further in view of Balbas et al. (Gene. 1996 Jun 12;172(1):65-9; reference of record) has been withdrawn in view of applicants' amendments and arguments filed 09/08/2006.

#### *Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
5. Claims 5, 9, 10, 11, 64, 65, 67, 69, 79, 82, and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.  
In claims 5, 9, and 69, parts (a)-(f) recite steps for performing the conversion of substrates to products but does not state that enzymes are involved in the conversions. This renders the claims vague and indefinite. Amending the claim, as in claim 1, to perform the conversions may overcome the rejection. For example, reciting the phrase "an enzyme that condenses acetoacetyl-CoA with acetyl-CoA to form HMG-CoA".

Claims 10, 11, and 79 recite several enzymes which are stated as "capable" of performing several enzymatic activities. However, it is unclear if these enzymes actually possess these functions since the claim recites the word "capable". Thus, the claims are indefinite. Claim 64,

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65, 67, 68, 82, 83 which depends from claims 10, 11, or 79 are also rejected because they does not correct this defect. Amending claims to recite that each of the enzymes performs their respective activities may overcome the rejection. For example reciting, as in claim 1, the phrase "an enzyme that condenses acetoacetyl-CoA with acetyl-CoA to form HMG-CoA".

***Claim Rejections - 35 U.S.C. § 112, 1st Paragraph***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-11, 13-21, 23, 61-85, and 87-102 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass methods for making an isoprenoid or an isoprenoid precursor including isopentenyl pyrophosphate (IPP) using transformed host microorganisms comprising one or more heterologous nucleic acids encoding various mevalonate pathway enzymes. Interpreted broadly, the claims encompass methods that do not require an enzyme that condenses acetyl-CoA to acetoacetyl-CoA.

The specification provides guidance and working examples using microorganisms having at least the heterologous nucleic acid encoding an enzyme that condenses acetyl-CoA to acetoacetyl-CoA as the first step in for synthesizing IPP. However, the specification does not provide guidance, prediction, and working examples methods that do not have at least the heterologous nucleic acid encoding an enzyme that condenses acetyl-CoA to acetoacetyl-CoA as the first step in for an isoprenoid or an isoprenoid precursor.

An undue amount of trial and error experimentation must be preformed to determine if

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the claimed methods can be used to make an isoprenoid or an isoprenoid precursor without the heterologous nucleic acid encoding an enzyme that condenses acetyl-CoA to acetoacetyl-CoA. This experimentation entails transforming microorganism with the various heterologous nucleic acids encoding mevalonate pathway enzymes and determining if any isoprenoid or an isoprenoid precursor can be synthesized without any heterologous nucleic acid encoding an enzyme that condenses acetyl-CoA to acetoacetyl-CoA. Thus, the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Amending the claims to recite that each of the methods must have the requirement of the enzyme that condenses acetyl-CoA to acetoacetyl-CoA as the first step in for synthesizing an isoprenoid or an isoprenoid precursor may overcome the rejection.

### *Conclusion*

8. No claim is allowed.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.
10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

  
TEKCHAND SAIDHA  
PRIMARY EXAMINER